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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/091,300	06/16/1998	WOLFGANG VON DEYN	5000-0103PUS1	4798

2292 7590 08/01/2011

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EXAMINER	
HAVLIN, ROBERT H	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
08/01/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)
	09/091,300	VON DEYN ET AL.
	Examiner	Art Unit
	ROBERT HAVLIN	1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,18,21-23,28-31,34-42 and 46-52* is/are pending in the application.

4a) Of the above claim(s) *17,18,22,23,31,34,38-42,46,49 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,28-30,35-37,47,48,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

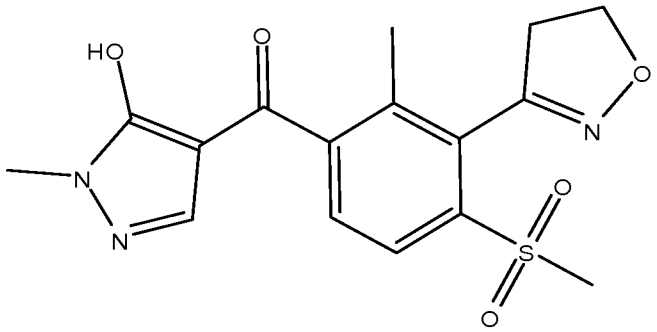
Status of the claims: Claims 17, 18, 21-23, 28-31, and 34-42, 46-52 are currently pending.

Priority: This application is a 371 of PCT/EP98/00069 (01/08/1998) and claims foreign priority to GERMANY 197 01 446.1 (01/17/1997). A certified copy of the foreign priority document is now of record (filed 5/19/2010).

Election/Restrictions

1. Applicant previously elected Group I (claims 18, 20, 21, 28-31, 34-42, and 46-52) and the species of claim 30 having the following structure:

4-[2-Methyl-3-(4,5-dihydroisoxazol-3-yl)-4-methylsulfonylbenzoyl]-1-methyl-5-hydroxy-1H-pyrazole



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Applicant argues on page 8 of the response that the burden on the examiner is not a criterion which applies in the determination of unity of invention and that the restriction requirement should be withdrawn. As detailed in the prior office action and below, the technical feature linking the claims is not a contribution over the prior art, and thus is not a special technical feature within the meaning of PCT Rule 13. Accordingly, the claims lack unity of invention, and restriction is proper.

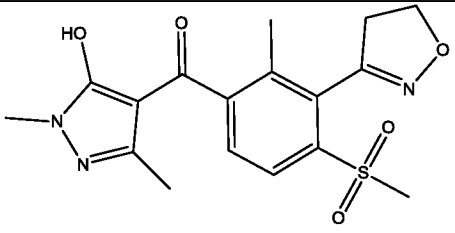
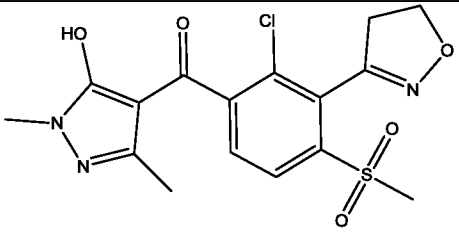
As detailed in the following rejections, the generic claim encompassing the elected species was not found patentable. Therefore, the provisional election of species is given effect, the examination is restricted to the elected species only, and claims not reading on the elected species are held withdrawn. Accordingly, the following claims not reading on the elected species or the elected group are withdrawn: 17,18,22,23,31,34,38-46,49 and 52.

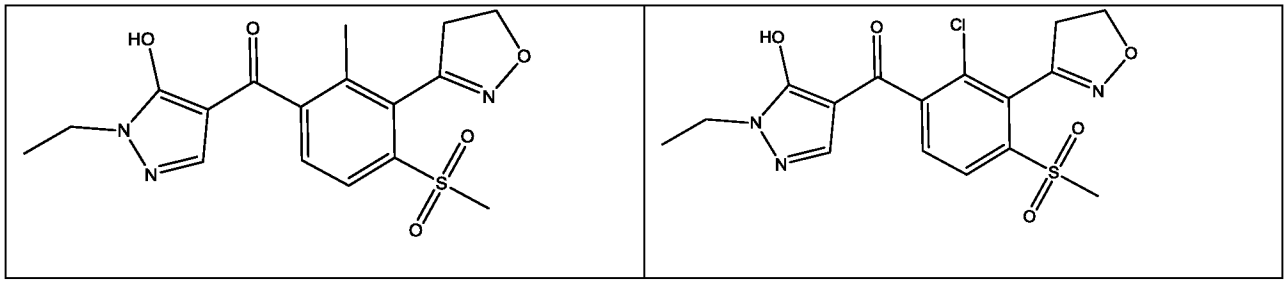
Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection through amendment, the amended Markush-type claim will be reexamined to the extent necessary to determine patentability of the Markush-type claim. See MPEP 803.02.

RESPONSE TO APPLICANT REMARKS

Claim Rejections – 35 USC 103

2. Claims 21,28-30,35-37,47,48,50,51 were rejected under 35 U.S.C. 103(a) as being unpatentable over Von Deyn et al. (WO 96/26206 [English equivalent US 5,846,907]) in view of Silverman, R. B. (The Org. Chem. of Drug Design and Drug Action, Academic Press, Inc.: San Diego, 1992, pp. 4-51).

CLAIMED INVENTION	PRIOR ART (von Deyn, comps. 5.4 & 5.5)
	

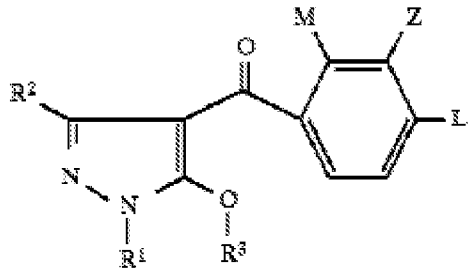


Applicant argues that the cited prior art does not render the claims obvious because Silverman fails to suggest modifying von Deyn in a manner that would replace the Chloro group with a methyl group. Applicant agrees that Silverman teaches bioisosterism by altering lead compounds through changing groups such as Chloro to Methyl as "classical isosteres," but argues that Silverman, when considered as a whole, does not teach that such a modification to arrive at an active compound would be a predictable result. In support of the argument Applicant cites excerpts that state "it may be a fairly random process to optimize potency …" and "[m]ajor pharmacological changes can occur with chain branching and homologation."

Regarding the first point, the statement merely indicates that the optimal isosteric replacement is somewhat subjective, however, it is well known in the art that substituting "classical isosteres" is expected to maintain the desired utility, thus the name "isostere."

Regarding the second point, this teaching is in the context of alkyl chain homoligation and not classical isosteres. Regardless, the standard is not that the result be absolutely predictable, but rather, the reasonable expectation of one of ordinary skill in the art. In this case, one of ordinary skill in the art would conclude, based in their own knowledge and experience exemplified by Silverman, that altering the compound of von

Deyn by making a classical isostere substitution to a methyl group at the chloro position would maintain von Deyn's utility. In fact, von Deyn specifically suggests that such a modification will be successful via the genus wherein "M" can vary to include methyl. Furthermore, Silverman teaches that such isosteric replacements by those of ordinary skill in the art is routine in the process of discovery of therapeutic compounds.

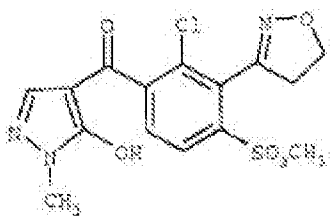
Applicant next argues that one of ordinary skill in the art seeking to modify the compounds of von Deyn would not have been advised by Silverman to do so with a reasonable expectation of success. The Examiner does not agree: von Deyn teaches a genus of compounds of the formula  where C1-6-alkyl is listed as a preferred alternative for M (col. 4 of the '907 patent), M as methyl is given as a specific example (col. 11), claim 4 lists methyl and chloro as among a few alternatives for M, and Tables 1-5 show that nearly all embodiments have M as Chloro or Methyl which shows the interchangeability of the two alternatives. Thus, one of ordinary skill in the art reading von Deyn would expect that modifying the Chloro group of compounds 5.4 and 5.5 to a methyl group would maintain the activity taught by the prior art. In addition, such a modification is within the scope of what von Deyn teaches as being an active compound. Furthermore, Silverman teaches that one of ordinary skill in the art routinely makes such modifications to optimize utility.

The Examiner has fully considered the two declarations of Witschel of October 21, 1999, and not found them persuasive as to the nonobviousness of the claims. Applicant states that the two declarations investigates herbicidal activity of compounds 5.4, 5.5, and 1.79 of the '907 patent and "the activity of those compounds within applicants' claims which come structurally closest to these prior art compounds."

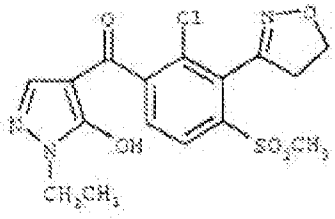
Applicant first cites Tables 1 and 2 of the Witschel declaration as showing that the prior art compounds cause "significant harm to the crop plant" and that the "structurally closes compound of applicants' invention are well tolerated." Furthermore, Applicant states that this effect "becomes even more pronounced" when compound 3.90 is compared to the prior art compound 5.5.

First, the compounds from Table 1 are as follows:

Table 1: Herbicidal action of compound 3.35 of the present invention and comparison compound no. 5.5 of WO 96/26,206 at an application rate of 125 and 62.5 g/ha of active ingredient (post emergence treatment in greenhouse)



compound 3.35

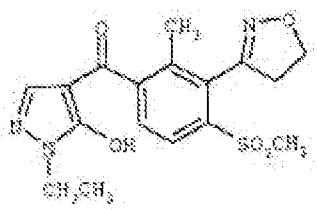


comparison compound no. 5.5 (WO 96/26,206)

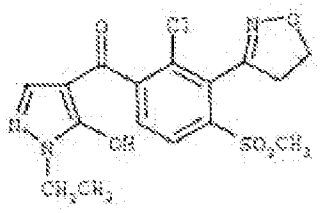
This is not a comparison of the claimed invention with the closest prior art and therefore is given little weight as a secondary consideration. Specifically, "compound 3.35" has a Chloro group where there should be a Methyl.

Second, Table 2 is reproduced below:

Table 2: Herbicidal action of compound 3.90 of the present invention and comparison compound no. 5.5 of WO 96/26,206 at an application rate of 62.5 and 31.2 g/ha of active ingredient (post emergence treatment in greenhouse)



compound 3.90



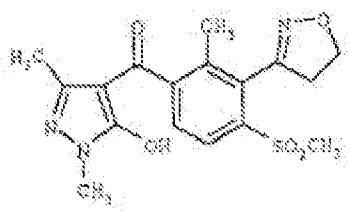
comparison compound no. 5.5 (WO 96/26,206)

Application rate	62.5 g/ha	31.2 g/ha	62.5 g/ha	31.2 g/ha
	Damage (%)			
Crop plant				
Zea mays	10	0	20	0
Unwanted Plants				
Abutilon theoprasti	80	80	75	60
Amaranthus retroflexus	80	80	70	60
Digitaria sanguinalis	100	100	100	98
Setaria italica	95	90	90	85

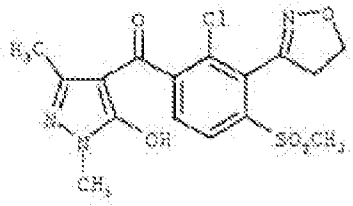
Applicant appears to argue that the differences of: 10/20 (compound 3.9 / prior art 5.5), 80/75, 80/70, 100/100, 95/90 and 0/0, 80/60, 80/60, 100/98, 90/85 are a “beneficial result” over the prior art, but nowhere argues that such a result is unexpected. In fact, examination of the “second declaration” by Witschel shows in tables 1-17 that such amounts of variation are what one of ordinary skill in the art would expect through modifications of the chemical structure.

Similarly, Table 3 is not argued as demonstrating an unexpected result and is in line with what one of ordinary skill would expect:

Table 3: Herbicidal action of compound A of the present invention and comparison compound no. 5.4 of WO 96/26,206 at an application rate of 62.5 and 31.2 g/ha of active ingredient (post emergence treatment in greenhouse)



compound A



comparison compound no. 5.4 (WO 96/26,206)

Application rate	62.5 g/ha	31.2 g/ha	62.5 g/ha	31.2 g/ha
	Damage (%)			
Abutilon theophrasti	90	85	85	65
Brachiaria platyphylla	90	80	80	65
Polygonum persicaria	95	70	75	65
Sinapis alba	100	100	90	85
Stellaria media	100	100	90	85

Finally, Table 4 has a cyano group on the isoxazole ring which is not part of the claimed invention and thus is given little weight in evaluating the nonobviousness of the claimed invention.

The 11 page second declaration of Witschel also does not establish the nonobviousness of the claims. The declaration does not compare the claimed invention with the closest prior art. Also, the declaration uses application rates that substantially differ from those used with the prior art compounds and thus of little probative value.

Applicant has failed meet their burden of establishing how the results described in the declarations are indeed unexpected and of practical and statistical significance. See MPEP 716.02(b).

In addition to the reasons discussed above, the comparisons of the claimed invention with the prior art does not include an associated error analysis for the measurements described. Therefore, the examiner cannot evaluate the statistical significance of the results. Specifically, error bars, +/- values, standard deviations, etc. are lacking in the measurement. Therefore, any alleged unexpected result cannot be determined.

At a minimum, the examiner recommends providing associated error analysis for all of the measurements, including confidence interval +/- values. In addition, comparisons at the same "Application rate" is recommended.

In conclusion, none of Applicant's arguments are persuasive and the rejection is **maintained**.

3. Claims 21, 28-30, 35-37, 47, 48, 50, 51 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,846,907 in view of Silverman, R. B. (The Org. Chem. of Drug Design and Drug Action, Academic Press, Inc.: San Diego, 1992, pp. 4-51).

Applicant does not make arguments different than those considered in the obviousness rejection supra. Therefore, this rejection is also **maintained**.

Conclusion

The claims are not in condition for allowance. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Primary Examiner, Art Unit 1626